RECURRENT HENOCH-SCHÖNLEIN PURPURA IN FAMILIAL MEDITERRANEAN FEVER

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Abstract- Familial Mediterranean fever (FMF) is a relatively rare disorder, characterized by recurrent self-limited attacks of fever and polyserositis. Diagnosis is made by clinical features, gene identification on chromosome 16 and clinical response to specific treatment. Different types of vasculitis have been reported in FMF. Henoch-Schönlein purpura (HSP) is one of them, usually with a benign clinical course. Repeated attacks of HSP have been rarely reported in FMF. This is the report of a 7-year-old girl who presented initially with recurrent fever and abdominal pain. After the primary diagnosis of FMF and appropriate treatment, she experienced two documented repeated attacks of HSP with severe renal involvement (crescentic glomerulonephritis) and protracted abdominal pain in the second one. Glomerulonephritis was controlled by methyl-prednisolone pulse therapy plus oral corticosteroid and azathioprine, but abdominal pain was resistant to steroids and revealed completely by intravenous immunoglobulin (IVIg) administration. In conclusion, it is suggested to consider the recurrence of HSP in cases with FMF to prevent irreversible renal complications. IVIg seems to be a good choice for the management of intractable abdominal pain of HSP.

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Key words: Familial Mediterranean fever, Henoch-Schönlein purpura, vasculitis, crescentic glomerulonephritis, intravenous immunoglobulin

INTRODUCTION

Familial Mediterranean fever (FMF) or paroxysmal polyserositis is an inherited disorder characterized by recurrent attacks of fever, abdominal pain, arthritis/arthralgia (1) and skin eruptions ranging from typical erysipelas-like erythema to non-specific purpuric rash or angioneurotic edema (2). It is more prevalent among Eastern Mediterranean populations, especially non-Ashkenazi Jews, Armenians, Turks and Arabs (1, 3). Responsible gene (MEFV) has been identified on chromosome 16, with more than 50 different point mutations (4, 5).

Various types of vasculitis such as polyarteritis nodosa (0.9%), Henoch-Schönlein purpura (HSP) (5%), febrile myalgia (6) and Behçet disease may be associated with FMF (7). It has been claimed that gene mutation and/or environmental factors are responsible for impaired control of inflammatory response and vasculitis in FMF (6, 8). HSP may be presented with its complete and benign clinical course in FMF, but recurrent episodes have been rarely reported.

In this article, we report a case of FMF with repeated attacks of HSP after the appropriate treatment.

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CASE REPORT

The patient was a 7-year-old girl with 18 months history of recurrent fever, abdominal and articular pain and occasional skin rash. Screening for FMF disease by cloning and gene identification on chromosome 16 was positive and treatment commenced effectively with colchicine.

A few months later, she experienced abdominal pain, joint swelling and petechial lesions on her legs and buttocks. Leukocytoclastic vasculitis was reported in skin biopsy in favor of HSP. She was treated conservatively with full recovery.

During the present admission, about 7 months later, she again had clinical manifestations of HSP. Her blood pressure was 110/70 mmHg. Laboratory exams revealed mild normochromic normocytic anemia, normal renal function, elevated ESR, negative CRP, glomerular hematuria with RBC casts and mild proteinuria. All of the serologic tests were negative. IgA level was high and serum complement level was normal. Class 3b crescentic glomerulonephritis of HSP with deposition of C3 and IgA in the mesangial area was documented in kidney biopsy specimen (Fig. 1). Therefore, it was the second documented episode of HSP in this case with FMF. The patient was treated with steroid pulse therapy along with oral prednisolone, azathioprine and colchicine. Majority of symptoms improved, except for protracted abdominal pain, which was completely controlled by intravenous immunoglobulin (IVIg) administration (200 mg/kg for 5 days).

We obtained informed consent to publish details of the patient's history.

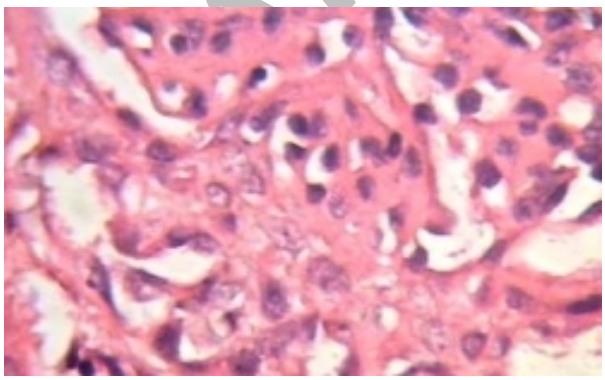

Fig. 1. Renal biopsy of the patient showing class 3b crescentic glomerulonephritis of Henoch-Schönlein purpura. (Hematoxylin-eosine staining, × 400).

DISCUSSION

Our patient was a case of periodic fever, abdominal pain and occasional skin eruptions. There are a few syndromes characterized by periodic fever (9, 10). One of them is hyperimmune globulin D fever with recurrent short episodes of fever, cervical lymphadenopathy, abdominal pain, arthralgia, skin rash, elevated acute phase reactants and IgD level (11). Tumor necrosis factor (TNF) associated syndrome is another disorder with intermittent fever, abdominal pain, myalgia, occasional rash, conjunctivitis, and unilateral periorbital edema, with increased level of acute phase reactants and a low serum level of TNF receptor. Another disease is periodic fever with aphthous stomatitis, pharyngitis, lymph adenitis and arthralgia, with spontaneous improvement within 4-8 years (9). None of the above diagnoses was compatible to our patient's.

Another syndrome characterized by periodic fever is FMF, which presents with fever and one or more symptoms of abdominal pain, arthralgia or arthritis and serosal involvement. Accumulation of C5a leads to acute attack in this disease. Diagnosis is based on clinical manifestation, genetic analysis and response to colchicine treatment, as our patient. Its specific gene (MEFV) has been localized to the short arm of chromosome 16, which mediates organ inflammation (4).

Renal involvement is usually in the form of AA amyloidosis in FMF (8). They are also at greater risk for developing nephrotic syndrome due to IgA and IgM nephropathy, mesangial proliferative glomerulonephritis (12) and renal complications of HSP (13).

HSP is a rare manifestation in FMF. It is considered to be an IgA mediated vasculitis with leukocytoclastic angitis. Clinical feature consist of arthralgia, abdominal pain, skin eruption and renal involvement. Each of these symptoms could be severe enough to mandate a serious treatment (14). In a study by Gershoni-Baruch *et al.*, occult FMF was identified in cases with HSP and they recommended closed monitoring of renal complications (15).

HSP may recur during a subsequent reactive phase of the disease (14) but, to our literature

review, repeated attacks of HSP have been rarely reported in FMF. In this case report, our patient experienced at least 2 documented episodes of HSP. She had also a severe and steroid resistant abdominal pain during the course of HSP, which was managed completely by IVIg administration. IVIg have been reported to be efficient in recurrent and intractable gastrointestinal symptoms of HSP (16, 17). Its mechanism of action is complex, including modulating the Fc receptors, interference with complement and cytokine network, and effects on activation and differentiation of T and B-cells (18). It has also a renoprotective effect (19) by reducing proteinuria, hematuria, leukocyturia, the histological index of renal biopsy and serum level of IgA and beta 2-microglobulin (20).

In conclusion, it is suggested to consider the recurrence of HSP in cases with FMF to prevent irreversible renal complications. IVIg seems to be a good choice in the management of intractable abdominal pain of HSP.

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